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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,704	08/25/2003	Brian Charles Gavin	PG3989US2	2717

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GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B475
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/647,704	GAVIN, BRIAN CHARLES	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/26/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-12 are presented for Examination.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed August 26, 2003 have been reviewed and considered, see the enclosed copy of PTO FORM 1449.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 5, 6, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "**treatment** of **specific condition** such as **asthma, chronic obstructive pulmonary disease (COPD), respiratory tract infection, and upper respiratory tract disease**", does **not** reasonably provide enablement for the "**prophylaxis or treatment** of **a clinical condition** in a mammal". The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for the **prophylaxis of a clinical condition** in a mammal for which a selective β2-adrenoreceptor agonist and/or anti-inflammatory corticosteroid is indicated, which comprises administering a therapeutically effective amount of a pharmaceutical formulation according to claim 1. The nature of the invention is extremely complex in that it encompasses the **actual prophylaxis** of **any clinical condition** (e.g. cancer) such that the subject treated with above composition does not contract **a clinical condition (e.g. cancer).** The Examiner equates the term "**prophylaxis" synonymous with the term "preventing**", and both circumscribe method of **absolute success**. Further, the **claims drawn to the treatment or prophylaxis of any clinical condition** is also doubted.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass **prophylaxis of a clinical condition** such as a complex **cell proliferation**

disorder (a clinical condition wherein anti-inflammatory corticosteroid is indicated) in humans which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prophylaxis the condition is minimal. All of the guidance provided by the specification is directed towards **treatment of specific clinical conditions rather than prophylaxis of any clinical condition** and treatment **of any clinical condition**.

Working Examples: All of the working examples provided by the specification are directed toward the **treatment of specific clinical conditions rather than prophylaxis of any clinical condition** and treatment of **any clinical condition**.

State of the Art: While the state of the art is relatively high with regard to treatment of a specific clinical condition such as cell proliferation disorders (i.e. cancer), the state of the art with regard to **prophylaxis** and **treatment of a clinical condition** is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prophylactic any clinical condition**, and treatment of **a clinical condition**. To the extent that the application is directed to a method of treating any clinical condition e.g. cancer cells in vivo, which is highly speculative, a greater amount of evidence is required

to show its operability in humans. It is to be noted that no data has been presented to establish that Applicants' compounds would act in the manner claimed as they relate to the treatment of any clinical condition in general. The difficulty in even treating specific clinical condition such as pancreatic, liver, colon and skin cancers is clearly known to the art as evidenced by Carter et al. reference at pages 361 to 367. This illustrates that the approximately 35 drugs tested only 3 shoed definite evidence of drug activity in the pancreases and only 4 in the colorectal and colon.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prophylaxis or treatment of **a clinical condition**, or **prophylaxis** of specific clinical condition in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of **prophylaxis/treatment** of **a clinical condition** or **prophylaxis** of a specific condition.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for **prophylaxis/treatment of a clinical condition**. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard **prophylaxis/treatment of a**

clinical condition with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding **prophylaxis/treatment of a clinical condition** with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to **prophylaxis/treatment of a clinical condition** in a mammal for which a selective B2-adrenoreceptor agonist and/or anti-inflammatory corticosteroid is indicated which comprises administering a therapeutically effective amount of a pharmaceutical formulation according to claim 1.

Therefore, a method for **prophylaxis/treatment of a clinical condition** in a mammal for which a selective B2-adrenoreceptor agonist and/or anti-inflammatory corticosteroid is indicated which comprises administering a therapeutically effective amount of a pharmaceutical formulation according to claim 1 is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 4-8, 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odeback et al. (1998) in view of Akehurst et al. (U.S.Patent No. 5,736,124) and further in view of Green et al. (1992), all of record.

Odeback et al. teach on the abstract, that a composition comprising budesonide and salmeterol is more effective than doubling the dose of budesonide in treating a clinical condition (i.e. asthma) as required by claims 6 and 12.

Odeback et al. do not explicitly teach the above composition with a **carrier** set forth in claim 1, the specific salt form of salmeterol (i.e. salmeterol xinafoate) set forth in claim 7, the route of administration set forth in claim 2, the specific propellants set forth in claim 4 and 10, the prophylaxis therapy set forth in claims 5 and 11, or the other specific clinical conditions (i.e. COPD, respiratory tract infection, upper respiratory tract disease) set forth in claims 6 and 12.

Akehurst et al. teach that budesonide and salmeterol (i.e. xinafoate salt as required by claim 7) are useful in inhalation therapy as required by claim 2 in treatment of respiratory disorders (clinical conditions) such as asthma as required by claims 6 and 12. (column 2, lines 23 through column 3, line 35, particularly, column 2, line 24, lines 29-31, line 42, line 65, line 68, column 3, line 1, line 33, lines 61-65). Akehurst et al. teach the formulation containing a medicament (i.e. salmeterol xinafoate, budesonide) formulated in propellant such as 1,1,1,2-tetrafluoroethane and 1,1,1,2,3,3,3,-heptafluoro-n-propane as required by claims 4 and 10, obtain a satisfactory dispersion without recourse to the use of any surfactant in the formulation or the necessity to pre-treat the medicaments prior to dispersal in the propellant and that salmeterol xinafoate is one of the preferred medicaments for inhalation formulation. (column 2, lines 6-13, lines 29-30, line 41, column 2 line 61 –column 3, line15, column 6-8 Examples 1,2,8 and 14).

Green et al. teach the effect of inhaled salmeterol xinafoate prevents exercise-induced asthma as required by claims 5 and 11 and produces significant bronchodilation. (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate the Odeback composition by incorporating the specific propellants set forth in claims 4 and 10 as a carrier as required by claim 1, and the specific salt form of salmeterol xinafoate set forth in claim 7 for treatment of asthma and the other specific clinical conditions set forth in claims 6 and 11 because Akehurst et al. teach those specific propellants have advantages in that they do not require one to pre-

treat the medicaments prior to dispersal in the propellant, and the specific salt form of salmeterol set forth in claim 7 is not only Akehurst's preferred medicament in inhalation formulation for treating asthma and respiratory related diseases in general but also produces significant brochodilation as taught by Green et al. One of ordinary skill in the art would have been motivated to employ the specified propellants set forth in claims 4 and 10 as a carrier in the Odeback composition in order to receive the expected benefit of achieving effective treatment of asthma as taught by Odeback without recourse to use of any surfactant, and/or without the step of pre-treating the medicaments as taught by Akehurst in order to save the cost and time in the manufacturing process. Moreover, the active agents utilized in Odeback composition are well known to be used for the treatment of respiratory disorders in general as taught by Akehurst et al. Therefore one would have been motivated to use the composition made from the combined teachings above for treatment of any respiratory related disorders (clinical conditions) set forth in claims 6 and 12 in general.

The route of administration set forth in claim 2 is obvious because budesonide and salmeterol are taught by Akehurst et al. to be administered as part of an inhalation composition in treatment of asthma. Moreover, Green et al. teach salmeterol xinafoate prevents exercise-induced asthma. Therefore, one would have been motivated to use the composition made from the combined teachings above for prophylaxis use as required by claims 5 and 11.

Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the composition taught by Odeback et al. to include

the specific propellants set forth in claims 4 and 10, as a carrier and specific salt of salmeterol (i.e. salmeterol xinafoate) set forth in claim 7 for the treatment of asthma and other respiratory related diseases set forth in claims 6 and 12 by an inhalation route as taught by Akehurst et al. and for the prophylaxis use as taught by Green et al.

Claims 1, 3, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odeback et al. (1998) in view of Akehurst et al. (U.S.Patent No. 5,736,124) and further in view of VanOort (U.S.Patent No. 5,647,347), all of record.

The teachings of Odeback et al. and Akehurst et al. described above and are applied as before.

Odeback et al. and Akehurst et al. do not teach the specific excipient set forth in claims 3 and 9.

VanOort teaches that an excipient, such as lactose, as required by claims 3 and 9 can be admixed with medicaments comprising salmeterol or budesonide in inhalation therapy. (column 4, lines 17-26).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate lactose in the Odeback et al's composition as modified by Akehurst et al. because VanOort teaches that lactose is compatible with salmeterol and budesonide in inhalation therapy and Odeback et al. and Akehurst et al. teach these compounds can be formulated in a single composition or singularly effective to treat asthma. One of ordinary skill in the art would have been motivated to make such modification in order to conveniently treat asthmatic patients with the composition

taught by Odeback modified by Akehurst et al. comprising a well known excipient (i.e. lactose) taught by Van Oort. Absent any evidence to contrary, there would have been a reasonable expectation of success in combining the composition taught by Odeback et al. as modified by Akehurst et al. with the excipient taught by Van Oort.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sreenivasan Padmanabhan
Supervisory Primary Examiner
Art Unit 1617

Jmk
September 20, 2006